SickKids® Pharmacogenomics Report

NAME: SAMPLE REPORT
Physician Copy for:
DOB: 01/01/2019
ID #: 219
Test report date: 17/06/2021
Case #: HSC-20210617

Consultation:

Focus Drugs:

Medication List:

Drug Summary:

Therapeutic Category	Use as directed	Caution - read recommendation	Consider alternatives
Anticoagulant		Clopidogrel	
		Warfarin	
Cardiovascular	Atorvastatin	Flecainide	
	Propafenone	Metoprolol	
	Simvastatin		
Dentistry	Cevimeline		
Endocrinology	Hormonal contraceptives for systemic use		
Gastroenterology	Dronabinol	Dexlansoprazole	
	Metoclopramide	Lansoprazole	
	Ondansetron	Omeprazole	
	Tropisetron	Pantoprazole	
Genetic disorder	Eliglustat		
Gout	Lesinurad		
Immunology	Tacrolimus	Azathioprine	
Infectious Diseases			Voriconazole
Neurology	Clobazam	Phenytoin/fosphenytoin	
	Siponimod		
	Tetrabenazine		

Therapeutic Category	Use as directed	Caution - read recommendation	Consider alternatives
Oncology		Mercaptopurine	
		Tamoxifen	
		Thioguanine	
Pain	Carisoprodol	Celecoxib	Piroxicam
	Oxycodone	Codeine	
		Flurbiprofen	
		Ibuprofen	
		Meloxicam	
		Tramadol	
Psychiatry	Aripiprazole	Desipramine	Amitriptyline
	Atomoxetine	Nortriptyline	Citalopram
	Brexpiprazole	Pimozide	Clomipramine
	Clozapine	Zuclopenthixol	Doxepin
	Fluvoxamine		Escitalopram
	Haloperidol		Imipramine
	Paroxetine		Trimipramine
	Perphenazine		Venlafaxine
	Risperidone		
	Sertraline		
	Thioridazine		
	Vortioxetine		

Genetic results:

Gene	Genotype	Phenotype	Status
CYP2C19	*1/*17	One functional allele and one increased-function allele	Rapid metabolizer
CYP2C9	*1/*3	One functional and one non-functional allele	Intermediate metabolizer
CYP2D6	*1/*4	One functional allele and one non-function allele	Intermediate metabolizer
CYP3A5	*3/*3	Two reduced-function alleles	Poor metabolizer
F5	WT/WT	Two normal risk alleles (WT = wild type)	Normal risk
SLCO1B1	*1/*1	Two functional alleles	Normal function
TPMT	*1/*3A	One functional allele and one reduced-function allele	Intermediate metabolizer
VKORC1	-1639 G>A GA	One normal functional allele and one reduced function allele	Reduced function

Drug/Dosing Recommendations:

Anticoagulant

Clopidogrel		Increased CYP2C19 enzyme activity may increase the conversion of clopidogrel to its active metabolite. Initiate therapy with the standard recommended starting dose. Patients with this genotype may have increased risk of bleeding.
Warfarin		Reduced CYP2C9 and VKORC1 enzyme activity may lead to increased sensitivity to warfarin. Per pharmacogenomic warfarin dosing algorithms a lower warfarin starting dose is recommended for the target INR 2-3. An updated dose estimation chart should be used to guide warfarin dosing. The Clinical Pharmacogenetics Implementation Consortium (CPIC) recommends that warfarin dosing follows either the Gage and/or IWPC algorithms, both of which drive the web-based algorithm found at warfarindosing.org. The genetic information below can be entered into the warfarindosing.org form to estimate the most appropriate therapeutic dose in patients new to warfarin. After filling in the "Required Patient Information", the following can be entered into the "Genetic Information" section of the form: VKORC1-1639/3673 = AG CYP4F2 V433M = Not available/Pending GGCX rs11676382 = Not available/Pending CYP2C9*2 = CC (Wildtype) CYP2C9*3 = AC (Heterozygous) CYP2C9*5 = CC (Wildtype) CYP2C9*6 = AA (Wildtype)

Cardiovascular

Flecainide		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects. Consider reducing the standard recommended starting dose by 25% and utilize ECG monitoring as well as therapeutic drug monitoring monitor to guide dose adjustments. This recommendation does not apply to the flecainide provocation test to diagnose Brugada syndrome.
Metoprolol		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects, in particular asymptomatic bradycardia. If a gradual reduction in heart rate is desired, or in the event of symptomatic bradycardia increase the dose in smaller steps and/or prescribe no more than 50% of the standard recommended dose. Otherwise, no action is required.
Propafenone		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug and its metabolites, which may increase the probability of side effects. Initiate therapy with the standard recommended starting dose. Utilize ECG monitoring and therapeutic drug monitoring to guide dose adjustments.
Atorvastatin		Normal SLCO1B1 transporter activity, which is related to a standard risk for statin-induced myopathy (muscle toxicity). Initiate therapy with the standard recommended starting dose.

Simvastatin		Normal SLCO1B1 transporter activity, which is related to a standard risk for statin-induced myopathy (muscle toxicity). Initiate therapy with the standard recommended starting dose.

Dentistry

Cevimeline		Reduced CYP2D6 enzyme activity may lead to increased levels of active drug. However, compared to normal metabolizers no significant difference in clinical effect or probability of side effects is expected. Initiate therapy with the standard recommended starting dose and monitor for side effects.

Endocrinology

Hormonal contraceptives for systemic use		Hormonal Contraceptives for systemic use: Use label recommended dosage and administration.

Gastroenterology

Lansoprazole		Increased CYP2C19 enzyme activity may lead to decreased levels of active drug and may affect clinical response. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.
Omeprazole		Increased CYP2C19 enzyme activity may lead to decreased levels of active drug and may affect clinical response. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.
Pantoprazole		Increased CYP2C19 enzyme activity may lead to decreased levels of active drug and may affect clinical response. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.
Dexlansoprazole		Increased CYP2C19 enzyme activity may lead to decreased levels of active drug and may affect clinical response. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.
Ondansetron		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug, which may increase the probability of side effects. There is insufficient data to allow for dose recommendations. Initiate therapy with the standard recommended starting dose and monitor for side effects.
Dronabinol		Reduced CYP2C9 enzyme activity may result in higher systemic concentrations and higher risk for side effects. Monitor for side effects.
Metoclopramide		Decreased CYP2D6 enzyme activity may lead to increased levels of active drug. However, compared to normal metabolizers no significant difference in clinical effect or probability of side effects is expected. Initiate therapy with the standard recommended starting dose.
Tropisetron		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug, which may increase the probability of side effects. There is insufficient data to allow for dose recommendations. Initiate therapy with the standard recommended starting dose and monitor for side effects.

Genetic disorder

Eliglustat		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects. The recommended dose also depends on concomitant medication use as well as hepatic and renal impairment. Use product monograph recommended dosage and administration.

Gout

Lesinurad		Reduced CYP2C9 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects.However, compared to normal metabolizers no significant difference in clinical effect or probability of side effects is expected. Initiate therapy with the standard recommended starting dose and monitor for side effects.

Immunology

Azathioprine		Reduced TPMT enzyme activity may lead to elevated levels of active drug, which increases the risk of side effects, in particular myelosuppression. Start with reducing the standard recommended starting dose by 30 - 80%. Utilize frequent laboratory monitoring, degree of myelosuppression and disease-specific guidelines to guide dose adjustments. Allow 2 - 4 weeks to reach steady state after each dose adjustment.
Tacrolimus		CYP3A5 non-expressors have a low enzyme activity, which is found in the majority of the population. Dosing recommendations for tacrolimus are based on CYP3A5 non-expressors. Initiate therapy with the standard recommended starting dose and utilize therapeutic drug monitoring to guide dose adjustments.

Infectious Diseases

Voriconazole		Increased CYP2C19 enzyme activity may lead to lower levels of active drug, which increases the probability of therapeutic failure. Consider an alternative agent that is not affected by CYP2C19 metabolism (e.g., isavuconazole, liposomal amphotericin B, posaconazole). If voriconazole cannot be avoided, consider increasing the standard recommended starting dose by 50% and utilize therapeutic drug monitoring to guide dose adjustments.

Neurology

Phenytoin/fosphenytoin		Reduced CYP2C9 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects. Consider reducing the standard recommended starting dose by 25% and utilize therapeutic drug monitoring to guide dose adjustments.
Clobazam		Increased CYP2C19 enzyme activity may lead to to lower levels of the active metabolite. However, compared to normal metabolizers no significant difference in clinical effect or probability of side effects is expected. Initiate therapy with the standard recommended starting dose and titrate based on clinical effect.

Tetrabenazine		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug and its metabolites. Current evidence suggests that the probability of side effects or clinical effect is not influenced by this genotype. Initiate therapy with the standard recommended starting dose.
Siponimod		Reduced CYP2C9 enzyme activity may lead to elevated levels of active drug. There is insufficient evidence that the probability of side effects is increased. Initiate therapy with the standard recommended starting dose.

Oncology

Tamoxifen		Reduced CYP2D6 enzyme activity decreases the conversion of tamoxifen to its active metabolite (e.g., endoxifen), which can result in reduced clinical effect. Consider an alternative treatment (e.g., aromatase inhibitors in post-menopausal women), or increase the standard recommended starting dose 1.5 to 2-fold and utilize therapeutic drug monitoring of endoxifen.
Mercaptopurine		Reduced TPMT enzyme activity may lead to elevated levels of active drug, which increases the risk of side effects, in particular myelosuppression. Start with reducing the standard recommended starting dose by 30 to 70 %. Utilize frequent laboratory monitoring, degree of myelosuppression and disease-specific guidelines to guide dose adjustments. Allow 2-4 weeks to reach steady-state after each dose adjustment. In setting of myelosuppression, and depending on other therapy, emphasis should be on reducing mercaptopurine over other agents.
Thioguanine		Reduced TPMT enzyme activity may lead to elevated levels of active drug, which increases the risk of side effects, in particular myelosuppression. Start with reducing the standard recommended starting dose by 30 - 50%. Utilize frequent laboratory monitoring, degree of myelosuppression and disease-specific guidelines to guide dose adjustments. Allow 2-4 weeks to reach steady state after each dose adjustment. In setting of myelosuppression, and depending on other therapy, emphasis should be on reducing thioguanine over other agents.

Pain

Codeine		Reduced CYP2D6 enzyme activity decreases the conversion of codeine to its more potent metabolite, which can result in reduced clinical effect. Initiate therapy with the standard recommended starting dose. If codeine is not effective, consider a dose increase or an alternative treatment that is not affected by CYP2D6 metabolism (e.g., acetaminophen, NSAID, morphine and non-opioid analgesics).
Oxycodone		Reduced CYP2D6 enzyme activity may lead to altered levels of active drugs and its active metabolites. Limited data is available to associate this variation with a weaker analgesic effect. Be alert to symptoms of insufficient pain relief. NOTE: Codeine, hydrocodone and tramadol are NOT good alternatives because their metabolism is also affected by CYP2D6 activity.
Tramadol		Reduced CYP2D6 enzyme activity may decrease the conversion of tramadol to its more potent metabolite, which can result in reduced clinical effect. If tramadol is not effective, try a dose increase and monitor for clinical effect or select an alternative treatment that is not affected by CYP2D6 metabolism (e.g., acetaminophen, NSAID, morphine and non-opioid analgesics). NOTE: Codeine, hydrocodone and oxycodone are NOT good alternatives because their metabolism is also affected by CYP2D6 activity.

Celecoxib		Reduced CYP2C9 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects. Consider using the lowest effective dosage for shortest duration consistent with individual patient treatment goals and monitor for side effects.
Carisoprodol		Increased CYP2C19 enzyme activity may lead to decreased levels of active drug. However, compared to normal metabolizers no significant difference in clinical effect or probability of side effects is expected. Initiate therapy with the standard recommended starting dose and monitor for side effects.
Flurbiprofen		Reduced CYP2C9 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects. Initiate therapy with lowest recommended starting dose and titrate dose upward to clinical effect or maximum recommended dose with caution.
Piroxicam		Reduced CYP2C9 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects. Select an alternative NSAID that is not affected by CYP2C9 metabolism (e.g., aspirin, ketorolac, naproxen and sulindac) or choose an NSAID metabolized by CYP2C9 but with a shorter half-life such as celecoxib, celecoxib, flurbiprofen, lornoxicam, and ibuprofen.
Ibuprofen		Reduced CYP2C9 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects. Initiate therapy with lowest recommended starting dose and titrate dose upward to clinical effect or maximum recommended dose with caution.
Meloxicam		Reduced CYP2C9 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects. Initiate therapy with 50% of the lowest recommended starting dose. Titrate dose upward to clinical effect or 50% of the maximum recommended dose with caution. Monitor for clinical effects and side effects. Alternatively, select an alternative NSAID that is not affected by CYP2C9 metabolism (e.g., aspirin, ketorolac, naproxen and sulindac) or choose an NSAID metabolized by CYP2C9 but with a shorter half-life such as celecoxib, celecoxib, flurbiprofen, lornoxicam, and ibuprofen.

Psychiatry

Amitriptyline		Increased CYP2C19 and reduced CYP2D6 enzyme activity may lead to altered levels of active drug and its metabolites. This may affect the clinical response and probability of side effects. Consider an alternative tricyclic antidepressant that is not affected by CYP2C19 metabolism (e.g., desipramine, nortriptyline). If amitriptyline cannot be avoided, utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.
Citalopram		Increased CYP2C19 enzyme activity may lead to decreased levels of active drug and may affect clinical response. Consider an alternative drug that is not predominantly metabolized by CYP2C19.
Clomipramine		Increased CYP2C19 and reduced CYP2D6 enzyme activity may lead to altered levels of active drug and its metabolites. This may affect the clinical response and probability of side effects. Consider an alternative tricyclic antidepressant that is not affected by CYP2C19 metabolism (e.g., desipramine, nortriptyline). If clomipramine cannot be avoided, utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.

Desipramine		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects. Consider reducing the starting dose by 25% and utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.
Doxepin		Increased CYP2C19 and reduced CYP2D6 enzyme activity may lead to altered levels of active drug and its metabolites. This may affect the clinical response and probability of side effects. Consider an alternative tricyclic antidepressant that is not affected by CYP2C19 metabolism (e.g., desipramine, nortriptyline). If doxepin cannot be avoided, utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.
Escitalopram		Increased CYP2C19 enzyme activity may lead to decreased levels of active drug and may affect clinical response. Consider an alternative drug that is not predominantly metabolized by CYP2C19.
Fluvoxamine		Reduced CYP2D6 enzyme activity may lead to increased levels of active drug. However, compared to normal metabolizers no significant difference in clinical effect or probability of side effects is expected. Initiate therapy with the standard recommended starting dose.
Imipramine		Increased CYP2C19 and reduced CYP2D6 enzyme activity may lead to altered levels of active drug and its metabolites. This may affect the clinical response and probability of side effects. Consider an alternative tricyclic antidepressant that is not affected by CYP2C19 metabolism (e.g., desipramine, nortriptyline). If imipramine cannot be avoided, utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.
Nortriptyline		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug, which increases the probability of side effects. Consider reducing the starting dose by 25% and utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.
Paroxetine		Reduced CYP2D6 enzyme activity may lead to altered levels of active drug. No significant difference in clinical effect or probability of side effects is expected. Initiate therapy with the standard recommended starting dose.
Sertraline		Increased CYP2C19 enzyme activity may lead to altered levels of active drug, which may affect the clinical response. However, compared to normal metabolizers no significant difference in clinical effect is expected. Initiate therapy with the standard recommended starting dose. If no response to therapy, consider alternative drug not predominantly metabolized by CYP2C19.
Trimipramine		Increased CYP2C19 and reduced CYP2D6 enzyme activity may lead to altered levels of active drug and its metabolites. This may affect the clinical response and probability of side effects. Consider an alternative tricyclic antidepressant that is not affected by CYP2C19 metabolism (e.g., desipramine, nortriptyline). If trimipramine cannot be avoided, utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.

Venlafaxine		Reduced CYP2D6 enzyme activity may lead to altered levels of active drug and its metabolites. This may affect the clinical response and probability of side effects. Consider an alternative drug that is not metabolized by CYP2D6 (e.g., citalopram or sertraline if compatible with CYP2C19 status). If venlafaxine cannot be avoided, consider reducing the starting dose and titrate according to the clinical response. If possible, utilize therapeutic drug monitoring of venlafaxine and the active metabolite to guide dose adjustments.
Aripiprazole		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug and its metabolites. Current evidence suggests that the probability of side effects or clinical effect is not influenced by this genotype. Initiate therapy with the standard recommended starting dose.
Atomoxetine		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects. Initiate therapy with the standard recommended starting dose and utilize therapeutic drug monitoring to guide dose adjustments. Consider to reduce the dose in case side effects occur and monitor for persistence of clinical effect.
Haloperidol		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug and its metabolites. There is insufficient evidence that the probability of side effects is increased. Initiate therapy with the standard recommended starting dose.
Risperidone		Decreased CYP2D6 enzyme activity may lead to increased levels of active drug. However, compared to normal metabolizers no significant difference in clinical effect or probability of side effects is expected. Initiate therapy with the standard recommended starting dose.
Thioridazine		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug, which may increase the probability of side effects. There is insufficient data to allow for dose recommendations. Initiate therapy with the standard recommended starting dose and monitor for side effects.
Brexpiprazole		Reduced CYP2D6 enzyme activity may lead to increased levels of active drug. However, compared to normal metabolizers no significant difference in clinical effect or probability of side effects is expected. Initiate therapy with the standard recommended starting dose.
Clozapine		Reduced CYP2D6 enzyme activity may lead to increased levels of active drug. Current evidence suggests that the probability of side effects or clinical effect is not influenced by this genotype. Initiate therapy with the standard recommended starting dose.
Pimozide		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects. Initiate therapy with no more than 80% of the standard maximum dose: adults 16 mg/day; children 0.08 mg/kg per day to a maximum of 3 mg/day.
Vortioxetine		Reduced CYP2D6 enzyme activity may lead to altered levels of active drug and its metabolites. Current evidence suggests that the probability of side effects or clinical effect is not influenced by this genotype. Initiate therapy with the standard recommended starting dose.
Zuclopenthixol		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug and increases the probability of side effects. Consider to reduce the standard recommended starting dose by 25% and titrate the dose based on clinical effect. Alternatively, select a drug that is not predominantly metabolized by CYP2D6 (e.g., flupentixol, fluphenazine, quetiapine, olanzapine or clozapine).

Perphenazine		Reduced CYP2D6 enzyme activity may lead to increased levels of active drug. However, compared to normal metabolizers no significant difference in clinical effect or probability of side effects is expected. Initiate therapy with the standard recommended starting dose.

Legend:

	Use as directed	Use label recommended dosage and administration
	Use with caution	Use with caution - read detailed recommendation for potential dose adjustment
	Consider alternatives	Select alternative treatment if possible -read detailed recommendation for details.

DISCLAIMER

Genotyping of CYP2C19, CYP2C9, CYP2D6, CYP3A5, F5, SLCO1B1, TPMT and VKORC1 will be carried out using the Agena MassARRAY® platform. Variants tested predict the following genotypes/haplotypes: CYP2D6*1,*2,*3,*4*,*5,*6,*7,*8,*9,*10,*11,*12,*14A,*14B,*15,*17,*18,*19,*20,*29,*41,*69; CYP2D6 Copy Number Variant (CNV) analysis is performed using the Agena Veridose CYP2D6 CNV panel, which detects both CNV's and hybrid alleles and includes 22 assays to interrogate 7 regions (5', exon 1, intron 2, intron 4, intron 6, intron 7 and exon 9) of the CYP2D6 gene; CYP2C19 *1,*2,*3,*4A,*4B,*5,*6,*7,*8,*17; CYP2C9 *1,*2,*3*4,*5,*6,*8,*11,*12,*13,*15,*25,*27; CYP3A5 *1,*2,*3*6,*7; VKORC1 *1,*2 (-1639G>A); F5 rs6025 (1601G>A); SLCO1B1 *1, *5 (rs4149056); TPMT *1, *2, *3A, *3B, *4.

Genetic variants not tested by this assay can contribute to an individual's efficiency of drug metabolism. This report is based on the technology and testing of certain variants listed above and may not fully take into account other factors that may affect drug sensitivity or efficacy such as co-medication, physical conditions, diet, smoking or the clinical context of the patient. The interpretation of this test may be affected by DNA rearrangements, blood transfusion, bone marrow transplantation or other rare events; these events can affect the testing and could cause false positive or false negative results. The interpretive report provided focuses on medications and genes with published pharmacogenomic practice guidance by professional organizations such as CPIC: Clinical Pharmacogenetics Implementation Consortium, DPWG: Dutch Pharmacogenetics Working Group, CPNDS: Canadian Pharmacogenomics Network for Drug Safety and FDA: U.S. Food and Drug Administration. The test used to prepare this report is a clinical investigational test; the test results are to be used for clinical research purposes only. Pharmacogenetic testing does not replace the need for therapeutic drug and clinical monitoring. It should be noted that the data interpretation outlined in this report is based on current understanding of genes and variants at the time of reporting. Patients are responsible for obtaining updates of this report, as necessary, in the future. The treating physician has ultimate responsibility for a patient's treatment plan, including treatment decisions made on the basis of this report. Neither the Hospital for Sick Children nor its employees or agents, shall have any liability to any person or entity with regard to claims, loss, damage arising, or alleged to arise, directly or indirectly, from the use of information contained in this report.